Pathology Section

Association of the Electrolyte Disturbances (Na^+, K^+) with the Type and Severity of the Malarial Parasitic Infection

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ABSTRACT

Background and Objective: Malaria is a life-threatening disease which is caused by malaria parasite. It is a major public health problem in India. The purpose of this study was to examine the possible changes in the electrolytes (Na+ and K+) in cases of malaria, on the basis of their severity.

Aim: The aim of this study was to determine the severity of hyponatraemia and hypokalaemia and their association with the severity of malaria in a large cohort of known patients of malaria, which was caused by the P.falciparum and the P.vivax species of Plasmodium.

Material and Methods: The serum sodium and serum potassium levels were analyzed in two cohorts, each comprising 400 diagnosed cases of P. Falciparum and P. Vivax (200 +200) malaria respectively, in a tertiary care hospital in Vadodara, Gujarat, India. The patients were divided into two groups of severe (200) and non-severe (200) cases of malaria, based on the WHO guidelines and criteria.

Statistical Analysis: The data from the study were analyzed separately by using the Statistical Package for Social Sciences. The results were presented as Mean ± SD. A p value of <0.05 were considered to be significant.

Results: The mean levels of serum sodium and serum potassium in the cases of P. Falciparum malaria were significantly reduced as compared to those in the cases of P.vivax malaria. Hyponatraemia and hypokalaemia were more common in P.falciparum than in P.vivax malaria. The levels of sodium and potassium are significantly reduced in the severe malaria cases as compared to those in the non severe malaria cases.

Conclusion: Hyponatraemia and Hypokalaemia are common in malaria and they are associated with severe falciparum and vivax malaria. Correction of the electrolyte imbalance in the severe cases is of great significance in the management of the patients.

Key Words: Malaria, Sodium, Potassium, Severity

INTRODUCTION

Malaria is life threatening disease, with nearly half of the world's population being vulnerable to this infection [1]. Malaria accounts for an estimated 2-3 million deaths annually and it is also responsible for the untold morbidity in approximately 300 -500 million people annually [1]. Four species of Plasmodium cause malaria in humans. These are P.falciparum, P.vivax, P.malariae and P.Ovale. P.falciparum is responsible for most of the deaths and most of the severe complications which result from malaria [2], which include cerebral malaria, anaemia and renal failure [3]

Malaria, is endemic in many states of India and even in Gujarat. It is a mosquito borne disease which spreads by the bite of the anopheles mosquito and rarely by blood transfusion. The species which are mainly prevalent in India are P.falciparum and P. vivax [4]. Electrolyte disturbances are known to be common in severe complicated malaria. Hyponatraemia has long been recognized as a complication of malaria. It had not been investigated previously how hyponatraemia was distributed among the various Plasmodium species, and its association with the severity of malaria is unknown.

The aim of this study was to determine the prevalence of hyponatraemia and other electrolyte imbalances and their association with the severity of malaria in a large cohort of patients with malaria which was caused by various Plasmodium species [5]. The pathophysiology of the hyponatraemia in malaria remains unclear, but several studies have suggested that an increased secretion of vasopressin, either appropriately or inappropriately, plays an important role [6].

Hyponatraemia is a decrease in the plasma sodium concentration to less than 135m.mol/l. The common causes are: integumentary loss (sweating, burns), gastrointestinal loss, renal loss, hepatic cirrhosis, etc.

The Grades of Hyponatraemia:

Mild: 131 to 135 m.mol/l, moderate: 126 to 130 m.mol/l and severe: < 126 m.mol/l [7].

Hyperkalemia is defined as an increase in the plasma potassium level to >5.0 m.mol/l. The common causes are: renal failure, hypo-aldosteronism, drugs like ACE inhibitors, etc. Hypokalaemia is defined as a decrease in the plasma potassium level to <2.5 m.mol/l. The common causes are burns, dehydration, etc. [8].

The aim of the study was to establish an association between the electrolyte imbalance, the type of the Plasmodium species and the severity of malaria.

MATERIALS AND METHODS

This was a prospective study which was carried out over a period of 1 year in the S.B.K.S.M.I. and R.C Dhiraj General hospital, Piparia, Vadodara, Gujarat, India. The Dhiraj hospital is a 1226 bedded, multispecialty hospital which caters to the rural populations of Vadodara and Waghodia. All the admitted patients with clinically suspected malaria (as per the WHO criteria) and who were willing to participate, were enrolled in the study. Before their enrolment in the study, the nature and purpose of the study were explained to all the participants. The diagnosis of malaria was made after the examination of the peripheral smears (thick and thin) and on the basis of the malarial antigen detection rapid card test.

There were 400 diagnosed cases of P. falciparum and P. vivax malaria (200 +200). The patients were divided into two groups of severe (200) and non severe (200) cases of malaria, based on the WHO guidelines and criteria. They are further divided on the basis of age into six groups.

Severe Malaria

The patients were considered as having severe P. falciparum malaria, if they met the predefined, modified World Health Organization (WHO) criteria for severe malaria on admission or during hospitalization ("severity criteria") :

- A Glasgow Coma Scale (GCS) score of < 11 (which indicated cerebral malaria) or
- Anaemia (haematocrit -< 0.20 L/L with a parasite count of > 100.000/µL) or
- Jaundice (serum bilirubin -> 50 µmol/L with a parasite count of > 100.000/µL)
- Renal impairment (urine output- < 400 mL/24 h and serum creatinine- > 25 µmol/L) or
- Hypoglycaemia (blood glucose -< 2.2 mmol/L) or
- Hyperparasitaemia (> 10% parasitaemia) or
- Shock (systolic blood pressure- < 80 mm Hg with cold extremities)
- Fulfilment of any one of the above criteria was considered as suggestive of severe malaria.

Inclusion Criteria

1. All the confirmed patients of malaria above 1year of age.
2. Willingness in giving an informed consent.

Exclusion Criteria

1. Unwillingness in giving an informed consent.
2. Already enrolled in the study.

For all the patients who were willing to participate in the study, their demographic profile, their complete history with vitals and relevant system examination with relevant laboratory investigations was recorded in a preformed proforma and they were subjected to the following investigations:

- Complete Blood Count (CBC) : [Hb, TC, DC and platelet]
- Peripheral Smear examination for the malaria parasite
- Serum billirubin
- Serum Creatinine
- Serum electrolyte (Na+, K+)

The methodology of the procedures to be followed:

1. CBC by using ("Sysmex KX-21 Three Part Differential Automated Haematology Analyser").
2. PSMP by the thick and thin smear methods; staining with the Giemsa stain.
3. Evaluation of serum billirubin and creatinin by using a semi-automated biochemistry analyser.
4. Evaluation of serum electrolyte (Na+, K+) by using a Prolyte fully automated electrolyte analyser.

Statistical Analysis: The data from the study was analyzed separately by using the Statistical Package for Social Sciences. The results were presented as Mean ± SD (Standard deviation) and a p value of <0.05 was considered as significant.

RESULTS

Age/ Gender	0-10 year	6–12 Year	13-20 year	21-30 year	31-50 year	>50 Year
	P.falciparum					
Male	19	14	34	26	23	2
Female	13	14	21	18	15	1
	P.vivax					
Male	11	19	30	16	56	1
Female	8	13	17	10	18	1

[Table/Fig-1]: Shows Age and Sex wise distribution of cases of P. Falciparum and P. vivax.

The above Table shows that males were more commonly affected than females. P.falciparum was more prevalent in the 13 to 30 years age group and P.vivax was more prevalent in the 31-50 years age group.

Gender	P.falciparum		P.vivax	
	Na+	K+	Na+	K+
Male	127.71 ±1.68	3.09 ± 0.43	132.25±1.71	3.54±0.41
Female	127.82 ± 1.26	3.07±0.41	132.48±1.61	3.56±0.43

[Table/Fig-2]: Shows comparison of Mean ± SD of serum Na+ and K+ level in P.falciparum and P.vivax.

The above Table shows that hyponataemia and hypokalaemia were more common in P.falciparum than in P.vivax malaria.

Electrolyte Level		Severe Cases of malaria	Non severe Cases of malaria	P -value
Na+	125-128	64	22	<0.05
	129-132	79	88	>0.05
	>133	57	90	>0.05
K+	<3	58	31	<0.05
	3-4	94	67	>0.05
	>4	48	102	>0.05

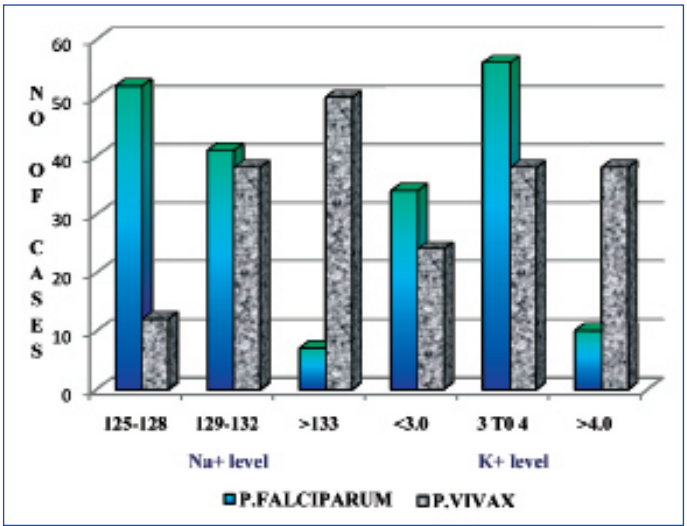
[Table/Fig-3]: Shows comparison of serum Na+ and K+ level in severe and non severe cases of P.Falciparum and P.Vivax.

The tables and the charts which are shown above revealed that hyponataemia and hypokalaemia were more common in the severe cases of malaria than in the non severe cases of malaria.

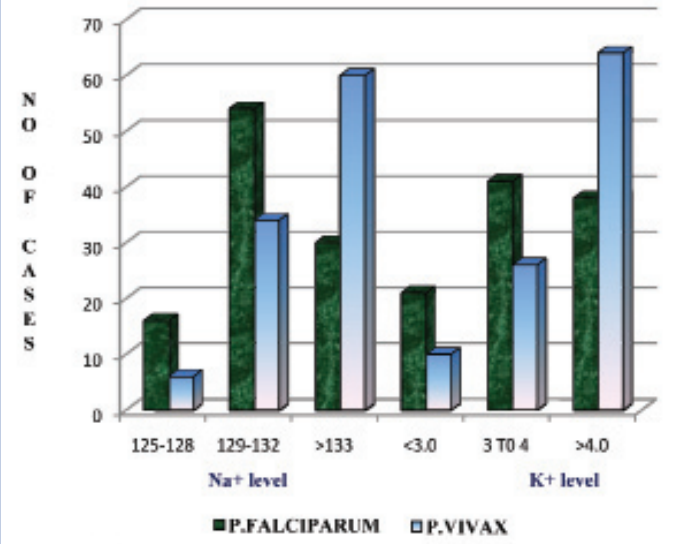
DISCUSSION

Malaria is a major cause of mortality and morbidity in the tropical regions in the world. An estimated 300-500 million persons suffer from malaria every year and more than 1 million die each year [9]. P.Falciparum is the species which is most commonly associated with the severe and complicated forms of this disease [10].

The results of this study showed that the malaria infection led to a reduction in the levels of both sodium and potassium. Hyponatraemia and hypokalaemia were more common and more



[Table/Fig-4]: Comparison of Na+ And K+ level in severe cases of malaria



[Table/Fig-5]: Comparison of Na+ and K+ level in non sever cases of malaria

severe in the severe cases of malaria than in the non severe cases of malaria. Hyponatraemia and hypokalaemia were also more common in the P.faciparum then P.vivax cases in both the severe and the non severe forms of malaria.

Fryatt RJ, et al suggested that the mild hyponatraemia that could be seen in the acute stages of malaria did not affect the mortality and the morbidity [11]. Some observations also suggested that in the non severe cases, there was a very mild reduction in the sodium and potassium levels.

Dworak et al (1975) [12] stated that there was a progressive decrease in the Na+ and K+ levels within 12 hrs of the parasite's occupancy, whereas Kakkilaya (2002) [13] reported mild hyponetraemia in the malaria patients. Ebele J Ikekpeazu et al (2010) [14] reported that there was a reduction in the Na+ and K+ level in the cases of malaria. Heindricks et al reported that the reduction in the K+ levels was because the host cells lost up to 75 to 80 % of their normal potassium content during the course of the malaria attack [15].

The observation that hyponatraemia which was seen in malaria was caused by any Plasmodium species, suggested that the hyponatraemia *per se* was unlikely to represent an exclusive feature of falciparum malaria, but that it merely reflected the effects of the severity of the disease.

A limitation of our study was that we did not compare the electrolyte levels between the hospitalized patients and the outpatients. But it seems unnecessary to assess the electrolyte levels in the outpatients with malaria due to the limitation of the costs and the measurement availability in the developing countries. Besides the clinical suspicion, the response to the anti-malarial treatment suffices in most of the outpatients.

The importance of assessing hyponatraemia that complicates severe malaria is in the fact that hyponatraemia is associated with adverse outcomes and that it should be specifically and aggressively treated.

CONCLUSION

Hyponatraemia and hypokalaemia are common in malaria and they are associated with the severe forms of falciparum and vivax malaria than with non severe malaria. Hyponatraemia and hypokalaemia are more common in P.falciparum than in P.vivax malaria.

This study drew attention to the need to manage the electrolyte derangements for the overall management of the malaria infections. From the clinical point of view, hyponatraemia is an indicator of the disease severity.

In general, serum electrolytes should be estimated in the malaria patients of all the age groups to prevent the complications which might result from electrolyte depletion, as these may produce grave consequences.

The precise patho physiological mechanisms of the hyponatraemia in malaria need to be further studied.

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